Early Journal Content on JSTOR, Free to Anyone in the World

This article is one of nearly 500,000 scholarly works digitized and made freely available to everyone in the world by JSTOR.

Known as the Early Journal Content, this set of works include research articles, news, letters, and other writings published in more than 200 of the oldest leading academic journals. The works date from the mid-seventeenth to the early twentieth centuries.

We encourage people to read and share the Early Journal Content openly and to tell others that this resource exists. People may post this content online or redistribute in any way for non-commercial purposes.

Read more about Early Journal Content at http://about.jstor.org/participate-jstor/individuals/early-journal-content.

JSTOR is a digital library of academic journals, books, and primary source objects. JSTOR helps people discover, use, and build upon a wide range of content through a powerful research and teaching platform, and preserves this content for future generations. JSTOR is part of ITHAKA, a not-for-profit organization that also includes Ithaka S+R and Portico. For more information about JSTOR, please contact support@jstor.org.

PUBLIC HEALTH REPORTS

VOL. 37 AUGUST 4, 1922 No. 31

PREPARATION AND ADMINISTRATION OF ARSPHENAMINE AND NEOARSPHENAMINE.

STANDARD INSTRUCTIONS FOR THE PREPARATION AND INTRAVENOUS ADMINISTRATION OF ARSPHENAMINE AND NEOARSPHENAMINE FOR USE BY THE MEDICAL DEPARTMENTS OF THE ARMY, OF THE NAVY, AND OF THE VETERANS' BUREAU, AND BY THE PUBLIC HEALTH SERVICE.

[Issued July 1, 1922, superseding all previous instructions.]

Reasons for Issuing Instructions.

Reactions following the use of arsphenamine and neoarsphenamine are still occurring in the Government services, although experience has shown that these reactions can be reduced to a minimum by the use of proper methods of procedure. Practically all serious reactions which have occurred in the Government services during the last five years have been specially investigated, and in nearly every instance it has been shown that the reactions were due (1) to some error in the technique of the preparation and administration of the drug or (2) to faulty examination of the patient, especially in relation to the effects of previous injections. In no case has it been possible to prove that the reactions have been due primarily to inherent toxicity of the drug itself. It therefore seems desirable to issue a complete set of instructions on technique.

Instructions are issued by each manufacturer, and they vary in some details with each product. In general, these instructions are satisfactory for the particular brand concerned; but as the same standard of relative nontoxicity is required by the Government for all brands, it is not considered desirable in these instructions to individualize the products.

The following instructions may seem unnecessarily explicit, and the technique outlined may differ from others which give satisfactory results. However, every essential statement contained herein is based on the results of the study mentioned above. The procedures given are designed to make the treatment safe and at the same time not to make the technique unnecessarily exacting or cumbersome for the clinician.

Medical officers are directed to follow these instructions and are cautioned that they will be held responsible for the untoward results following the use of procedures which are essentially different.

Any of the specified apparatus which is not on hand will be furnished upon request through regular channels.

Choice of Drug.

Although neoarsphenamine is more popular than arsphenamine, on account of ease of preparation and administration, which constitutes a real advantage under some circumstances, attention is called to the fact that neoarsphenamine is a much less constant and less reliable preparation than arsphenamine.

Not only do certain batches of all brands of neoarsphenamine show a tendency to deteriorate with age but there is also a pronounced irregularity in the therapeutic activity of different batches of neoarsphenamine, regardless of the age and source of the preparations. As a result of these variations, the physician may obtain a much less satisfactory therapeutic result than when arsphenamine is used. Arsphenamine, regardless of age, brand, or lot number, shows a more uniform therapeutic activity. It is probably, also, inherently more potent. Arsphenamine should, therefore, be used whenever practicable, and neoarsphenamine should be reserved for situations in which it is difficult to give arsphenamine.

Other members of the arsphenamine series are considered to be still in the experimental stage and not for routine use.

In regard to different brands, any product which has passed the requirements of the United States Public Health Service may be used. The labels of duly licensed products bear imprint to this effect and the license number.

Arsphenamine.

I. LICENSED PRODUCTS.

The following firms have been licensed by the Treasury Department to manufacture or to import arsphenamine:

A. LICENSED TO MANUFACTURE.

Name of firm and address.	Name of trade product.
Dermatological Research Institute, 1720 Lombard Street, Philadelphia, Pa.	Arsenobenzol.
Diarsenol Company (Inc.), Buffalo, N. Y.	Diarsenol.
Mallinckrodt Chemical Works, St. Louis, Mo.	Arsphenamine.
H. A. Metz Laboratories (Inc.), 122 Hudson Street.	Salvarsan.
Powers-Weightman-Rosengarten Co., Philadelphia, Pa.	Arsenobenzol Billon.
E. R. Squibb & Sons, New Brunswick, N. J.	Arsphenamine.

B. LICENSED TO IMPORT.

Name of firm and address.	Name of trade product.
Farbwerke, vorm. Meister Lucius und Brüning, Hoechst-am-Main, Germany	Salvarsan.
Poulenc Frères, 92 Rue Vieille-du-Temple, Paris, III, France.	Arsenobenzol Billon.

II. METHOD OF INJECTION.

Only the gravity method should be employed in administering arsphenamine.

III. MATERIALS REQUIRED.

A. Erlenmeyer flasks, 500 to 1,000 c. c. capacity.

B. Funnels, glass, 4-inch.

C. Cylinders, graduated, 500 to 1,000 c. c. capacity.

D. Gravity apparatus, consisting of—

1. Gravity graduated glass cylinders, 300 c. c. capacity; long graduations at the 100 c. c. marks; medium long graduations every 25 c. c.; short graduations for each 5 c. c.; the zero point to be at the top and the 300 mark to be at the bottom of the cylinder.

2. Rubber tubing, pure gum, heavy wall, inside diameter, 5/32-inch (about 4 mm.), of lengths to limit height of the cylinder to 3 feet above the patient's arm.

Caution: Before being used the first time the tubing should be filled with normal sodium hydroxide solution for not less than six hours. It should then be thoroughly rinsed in water, sterilized by boiling, and then thoroughly rinsed with sterile water again just before using.

3. Needles with slip joint, 19 standard gauge, medium bevel, length of cannula 1½ inches. While not necessary, the Fordyce type of needle is a great convenience. The correct gauge is highly important, as it influences the rate of flow. Proper care of the needles is important. They should be cleansed immediately after use, and precautions taken to prevent rust. Just before sterilization, the point should be freshened on a stone, if necessary. A dull needle tends to make a dissatisfied patient.

4. Glass tubing, 6 mm. in diameter, for windows, which should be inserted in the rubber tubing so as to be a few inches from the lower end.

5. Adapters for attaching needles to end of tubing. These may be of metal or glass. If of glass they will serve as extra windows as well as adapters.

6. Pinch cocks (Mohr's) for cutting off the flow, to be applied a short distance above the needle.

E. Sterile gauze, cut in small squares, for filtering the solution.

F. Sterile freshly distilled water. This water should be distilled in glass or block tin and should be sterilized immediately by autoclaving or boiling in Erlenmeyer flasks. These flasks should be stoppered with a gauze-wrapped cotton plug and capped with paper or tin foil. Preparation of the water preferably should be carried out on the day before use, so that it will be both fresh and cool at the time needed.

G. Sterile salt solution. This should be made with water prepared as above and chemically pure sodium chloride. Sterilization should be carried out as given above. The strength of the salt solution should be the usual 0.85 per cent. The use of salt solution in the place of distilled water for the dilution is considered a refinement which is not necessary in routine work, but it may have some advantages, since a solution of arsphenamine in distilled water is not isotonic.

H. Normal sodium hydroxide volumetric solution, U. S. P. IX, p. 573. Enough of this can be prepared at one time to last for a month or longer, provided it is kept in a rubber stoppered wax- or paraffin-lined bottle. There is danger of deterioration on account of absorption of CO_2 from the air and of reactions with the glass container. A wax-lined bottle can be prepared by placing wax or paraffin in a bottle, sterilizing with dry heat, and spreading the melted wax by rotation over the inside of the bottle as it is cooling. If precipitate is found in the alkali, it is probably an evidence of deterioration of the solution, which should be discarded. For use in large clinics, a 2-liter bottle, protected from the action of the alkali and of the atmospheric CO_2 and set up with an automatic measuring burette, is a great convenience and will insure the safe-keeping of the alkali for a long period.

I. Burette or pipette. A graduated burette or pipette for accurately measuring the alkali.

All the glassware mentioned above should be of chemical standard. All apparatus should be surgically clean, freshly sterilized, and cool at time of using. The apparatus should be sterilized by dry heat or autoclave, with the exception of the tubing and the needles, which should be boiled.

If the medical officer has any doubt about being able to obtain pure normal sodium hydroxide solution, the same will be supplied on request to the Army Medical School, the Naval Medical School, or to the Hygienic Laboratory, Washington, D. C.

IV. INSPECTION OF DRUG.

A. Note and record manufacturer, lot number, and particularly the dosage stated on the label. In this connection it is a great convenience, and more economical, to employ dosages which are just sufficient to make up the unit batch of solution desired; e. g., if 10 doses of 0.4 gram are made up at a time, use ampules containing 4 grams. An ampule containing 10 doses is the largest that should be used.

B. Examine ampules critically and do not use any which are cracked or in which the powder is not freely mobile and is not of a pale yellow to a lemon-yellow in color. Forward any suspected ampules with explanatory letter directly to the Hygienic Laboratory, Washington, D. C., for examination.

C. The ampules, having satisfactorily passed preliminary inspection, should be immersed in 95 per cent alcohol, primarily to detect any minute cracks in the glass not visible on preliminary inspection and also to cleanse the ampule. Lay ampules on sterile towel to dry or wipe off alcohol with sterile gauze.

V. PREPARATION OF SOLUTIONS.

A. The amount to be prepared at one time will depend on the number of patients, but unit batches of more than 10 average doses should not be prepared.

B. Place in Erlenmeyer flasks about 10 c. c. of freshly distilled sterile water for each decigram of arsphenamine to be used; e. g., 100 c. c. for 1 gram. Open ampule and sprinkle—do not dump—contents on surface of water. The temperature of the water is of great importance. For all brands of arsphenamine, except for arsenobenzol manufactured by the Dermatological Research Institute, the water should be at room temperature and, as a rule, the drug should go into solution, with little or no agitation, within a few minutes. A slight amount of shaking is permissible with any product, but shaking should always be kept at a minimum.

Exception: The arsphenamine manufactured by the Dermatological Research Institute requires either hot water alone, or it can be dissolved in cold water if the powder is first thoroughly moistened with ethyl alcohol (about 1 c. c. to 0.6 gram). This amount of alcohol is harmless. In either case it is essential, immediately after contact with the water, to shake the powder vigorously for a few seconds in order to prevent the formation of gummy masses. After this shaking it should stand until completely dissolved and until the solution is cool.

When the arsphenamine has completely dissolved, forming a perfectly clear solution with an absence of any gelatinous particles when viewed by transmitted light, it is ready for alkalinization. If for any reason the arsphenamine fails to form a perfect solution, it must be discarded.

C. Correct alkalinization is extremely important; failure to alkalinize properly causes more reactions than any other error connected with the use of arsphenamine.

1. The exact method consists in the addition all at once of 0.85 c. c. normal sodium hydroxide solution for each 0.1 gm. of arsphenamine used; e. g., 8.5 c. c. for 1 gm. of drug. This is the correct amount necessary to form the disodium salt of arsphenamine (see V, p. 1873), the form which is best tolerated by the patient.

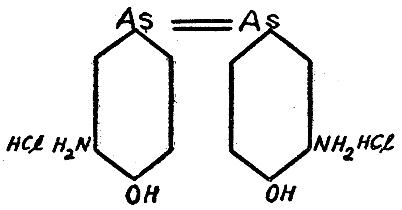
2. Approximate method of alkalinization. An exception to the rule that only standardized normal alkali should be used may be made in case this is not obtainable. Under such circumstances, the exact concentration of alkali being unknown, the operator should keep in mind the following facts: Arsphenamine as it appears on the market is the dihydrochloride of the arsphenamine base (see I, p. 1873), which is soluble in water; but the solution is strongly acid and highly toxic. Upon the gradual addition of sodium hydroxide a precipitate at once begins to form and then redissolves. This property of the drug, not understood by some physicians, has caused them to mistake the end point. This mistake is especially likely to occur when the operator thinks he is using a 15 per cent solution, when in reality the solution is only 4 or 5 per cent. The drug when injected in this still strongly acid state, the monohydrochloride (see II, p. 1873), produces serious reactions.

When a little over one-fourth of the amount of alkali indicated under (1) has been added, the precipitate no longer redissolves. From this point on, until there has been added almost three-fourths of the amount of alkali necessary to form the disodium salt, the precipitate remains and does not redissolve on shaking (see III, p. 1873). But when three-fourths of the total amount necessary has been added, the precipitate redissolves (see IV, p. 1873).

It is at this point, when just enough alkali has been added to dissolve the precipitate, that the solution has very frequently been injected. *This solution of the monosodium salt is the most frequent cause of reactions.* At this point 75 per cent of the correct amount of sodium hydroxide solution has been added, and hence an additional one-third of the total amount of alkali used up to this point should now be added (see V, p. 1873). This last addition is the remaining 25 per cent of the correct amount corresponding to a total of 0.85 c. c. per 0.1 gm. of standardized $\frac{N}{1}$ NaOH solution as mentioned under (1) above; e. g., if 3.3 c. c. of an unknown solution were required for completely clearing a

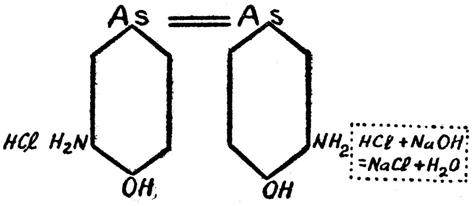
The Chemical Transformation of Arsphenamine into its Disodium Salt for Intravenous Administration by the Addition of Sodium Hydroxide.

I. ARSPHENAMINE DIHYDROCHLORIDE



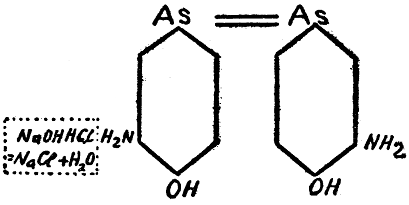
I. Arsphenamine (dihydrochloride). This is the drug as it appears on the market. It is soluble in distilled water, strongly acid to litmus, highly toxic, and must not be injected.

II. ARSPHENAMINE MONOHYDROCHLORIDE



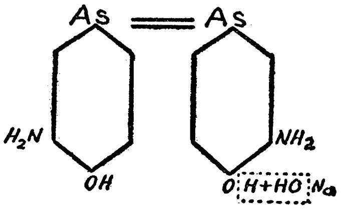
II. Arsphenamine monohydrochloride is formed when one-fourth the amount of sodium hydroxide necessary to form the disodium salt has been added, or 0.85 c. c. of normal sodium hydroxide per 0.4 gram of arsphenamine. It remains in solution, is still strongly acid to litmus, is highly toxic, and must not be injected.

III. ARSPHENAMINE BASE



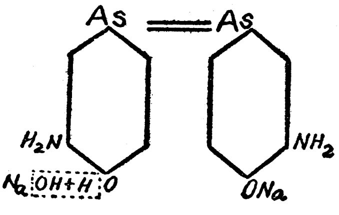
III. The base is formed when one-half the amount of sodium hydroxide necessary to form the disodium salt has been added, or 1.70 c. c. of normal sodium hydroxide for 0.4 gram of arsphenamine. A heavy insoluble precipitate is formed. This suspension must not be injected.

IV. MONOSODIUM ARSPHENAMINE



IV. The monosodium salt of arsphenamine is formed when three-fourths the amount of sodium hydroxide necessary to form the disodium salt has been added, or 2.55 c. c. of normal sodium hydroxide per 0.4 gram of arsphenamine. It is just soluble in water, and forms an unstable, slightly alkaline solution, which must not be injected.

V. DISODIUM ARSPHENAMINE



V. The disodium salt of arsphenamine is formed when the final fourth of the full amount of normal sodium hydroxide necessary has been added, or 3.4 c. c. of normal sodium hydroxide for 0.4 gram of arsphenamine. This amount is one-third more than the amount used for the monosodium salt IV. This form is a stable alkaline solution. It is the only form in which the drug should be injected.

solution containing 2 gms. of arsphenamine, 1.1 c. c. more should be added. With a thorough understanding of the above, the operator may roughly standardize his alkali against the arsphenamine. No two brands of arsphenamine vary greatly in the amount of alkali required, whereas various alkali solutions vary in strength by several hundred per cent.

The P_h of a proper solution is about 10, and it is impossible to buffer it to neutrality by common buffers without precipitation. Moreover, the alkaline solution is well tolerated if given slowly and well diluted.

3. "*Haphazard method*" of alkalinization, or *drop method.* This is mentioned only to condemn it. It is inconceivable that the operator will be unable to secure some sort of a graduated measuring device in order to measure the alkali instead of guessing at the amount. Numerous reactions from underalkalinization have occurred with this method, particularly where several doses of the drug are prepared at one time. The alkali has been added with a dropper until clearing occurred, and then a few additional drops have been added regardless of whether the solution contained 1 or 10 doses. Less frequently overalkalinization has also occurred. The injection of an overalkalinized solution causes pain along the vein, and thrombosis.

D. *Filtration and dilution to proper strength* of the alkalinized solution.—With sterile forceps place 4 layers of sterile gauze in the funnel. Wash with sterile water. Pour alkalinized solution of arsphenamine through this gauze into a graduated cylinder and then rinse the filter with enough sterile distilled water to bring the total for each decigram of drug up to 25 c. c.; e. g., for 1 gram of arsphenamine 250 c. c. of solution should be made. This washing of the drug through the filter with the water insures full dosage. If a saline solution is desired, it is used at this point in place of the distilled water, at usual strength, 0.85 per cent.

E. *Time the solution should be allowed to stand.*—The *properly alkalinized, filtered,* and *diluted* solution should now stand for at least 30 minutes before being injected, to allow completion of the chemical reactions. The toxicity is considerably reduced by this delay. The solution may stand as long as three hours without undergoing any increase in toxicity, provided it is protected from the air, not shaken, and provided the temperature does not exceed 30° C. The solution is now ready for administration.

F. *Temperature.*—Thirty degrees C. is the correct temperature at which the drug should be introduced; in no case should it be warmed above this point.

G. *Dosage.*—As a rule the initial dose should be small. The average dose used is about 0.4 gram for 150 pounds body weight, but no hard and fast rule can be laid down; each case should be considered individually by the clinician. When a radical cure is being sought and the patient tolerates the injections well, full doses should be given.

VI. ADMINISTRATION.

A. Emphasis should be laid on the complete physical examination preliminary to administering arsenical treatment, for evidence of renal, cardiovascular, or visceral changes, in the presence of which it should be used cautiously. Weekly urinalyses should be made during treatment. The patient should be questioned concerning any reactions following the last treatment, with special reference to any toxic skin eruptions as danger signals against further treatment. Any evidence of an exfoliative dermatitis is an *absolute contraindication* against any further treatment with any arsenical. Evidence of jaundice should also be looked for and, if present, is an indication for caution. In late cases the possibility of a Herxheimer reaction following a large injection should be remembered. This may be fatal should vital structures be involved. *Each patient should receive individual consideration.*

B. *Preparation of patient.*—The patient should be given a mild cathartic the night before and should eat no food within two or three hours before the injection. Only a light meal should be taken a few hours following the injection. Ambulatory patients should rest for a short time after the injection. If large doses are being given, the patient preferably should be kept in bed until the following morning.

C. The patient should be placed in a recumbent position.

D. The gravity apparatus should be arranged to provide a column of solution not over 3 feet in height. The tubing should be rinsed with sterile water; then the cylinder and tubing should be filled with the solution and the air expelled by lowering the end of the tube below the level of the fluid in the cylinder. Apply pinch cock.

E. Select a suitable vein in either arm and sterilize the overlying skin by applying tincture of iodine, which should preferably be removed after a minute or two with 95 per cent alcohol.

F. Apply rubber turniquet.

G. Insert needle, bevel up, in two stages (first through the skin, second into the vein), and allow a few drops of blood to escape to indicate entrance to the vein. The needle should be slid well into the vein in order to avoid escape of the point from the vein on further slight manipulations. Now connect adapter attached to gravity apparatus. Open pinch cock and snap it over the window.

H. *Rate of injection.*—If the specifications as to the gauge of needle, etc., have been followed, the correct rate of injection is practically insured, i. e., by the size of the needle and the length of the tube; however, this should not be taken for granted, but the exact time should be observed, and in no case should the rate exceed 25 c. c. in one minute or 0.4 gram dose in four minutes; five minutes is preferable. A graduated sand glass which runs for five minutes is a convenient timer. The rate of flow should be even as well as slow. Should patient show any signs of reaction, stop. It is highly desirable, in sensitive patients, to wait a minute or two after injection of first 0.1 gram before proceeding with rest of injection. When the necessary amount has been injected, cut off flow with pinch cock, disconnect tubing, allow a few drops of blood to escape, and then withdraw needle and place sterile gauze over the puncture, instructing the patient to hold it there for a few minutes. If another injection is to be given and there is any suspicion of contamination of the tubing with blood, empty cylinder and start over with a new sterile tube.

VII. REACTIONS.

Following the above methods, reactions should be rare. If a serious reaction does occur, a complete account should be forwarded to the Surgeon General, including clinical history, dose injected, lot number, and manufacturer of the drug. Samples should also be sent of the same lot of drug; also samples of the sodium hydroxide, distilled water, and saline used for purposes of investigation.

The prevention and treatment of reactions is very important. A discussion of this subject is not undertaken here, except to call attention to general hygiene, diet, foci of infection, dosage, etc., as well as care in preparation and administration of the drug in prophylaxis of these reactions. Patients that continually show immediate reactions should receive prior administration of atropine or divided doses of arsphenamine or combinations of both. In the clinical control of the immediate or nitritoid types of reactions, the chief preparation of value is epinephrin $\frac{1}{1000}$, about 1 c.c. intramuscularly. This is also of value in the very severe type of reaction—hemorrhagic encephalitis. In the severe types of skin reactions, as exfoliative dermatitis, rapid alkalinization of the patient is indicated. In all these delayed types of arsenical poisoning excellent results are said to be derived from the use of sodium thiosulphite given by mouth or intravenously.

Neoarsphenamine.

I. LICENSED PRODUCTS.

The following firms have been licensed by the Treasury Department to manufacture or import neoarsphenamine:

A. LICENSED TO MANUFACTURE.

Name of firm and address.	Trade name of product.
Dermatological Research Institute, 1720 Lombard Street, Philadelphia, Pa.	Neoarsphenamine.
Diarsenol Co. (Inc.), Buffalo, N. Y.	Neodiarsenol.
H. A. Metz Laboratories (Inc.), 122 Hudson Street, New York City	Neosalvarsan.
Powers-Weightman-Rosengarten Co., Philadelphia, Pa.	Novarsenobenzol Billon.
E. R. Squibb & Sons, New Brunswick, N. J.	Neoarsphenamine

B. LICENSED TO IMPORT.

Farbwerke, vorm. Meister Lucius und Brüning, Hoechst-am-Main, Germany	Neosalvarsan.
Poulenc Frères, 92 Rue Vieille-du-Temple, Paris, III, France	Novarsenobenzol.

II. METHOD OF INJECTION.

The use of the gravity method is strongly recommended, especially in clinics where a considerable number of doses are to be given. It was demonstrated in one clinic that the average time required to give 100 injections was reduced, without changing the personnel, when the gravity method was substituted for the syringe method, and a high percentage of reactions, due directly or indirectly to the syringe method, also ceased to occur. With the gravity apparatus arranged to deliver a dose in about four minutes, one operator was able to run two tables much more easily than one table with the syringe method.

It is recognized, however, that there are circumstances in which the syringe method is indicated, as in the field, where apparatus must be reduced to a minimum. Under these circumstances the use of neoarsphenamine by the syringe method is a valuable therapeutic measure. It fills a need, but technically is inferior to the gravity method; and, therapeutically, neoarsphenamine given by either method is inferior to arsphenamine given by the gravity method.

III. APPARATUS REQUIRED.

A. When the gravity method is to be used:
  1. Gravity apparatus (see Arsphenamine, III–D).
  2. Erlenmeyer flasks, 50–300 c.c.
  3. Funnels, glass, 2-inch.
  4. Sterile gauze.

5. Graduated glass cylinders, 100 to 500 c. c.
6. Sterile distilled water (see Arsphenamine, III–F).
7. Saline, 0.85 per cent (see Arsphenamine, III–G).

B. When syringe method is to be used:

As above, except in place of gravity apparatus.

1. 10 to 50 c. c. all-glass syringes.
2. Rubber tubing, short, with adapters connecting syringe and needle.
3. Needles, 25 standard gauge, medium bevel.

IV. INSPECTION OF DRUG.

An even more critical examination should be made than in case of arsphenamine, as neoarsphenamine occasionally decomposes in the ampule, even when no cracks are present. The powder should be freely mobile and lemon-yellow to canary-yellow in color. When it approaches a red color, is distinctly lumpy or solidified, do not use, but forward samples to the Hygienic Laboratory for examination.

Immerse in alcohol the ampules which have passed inspection, to further eliminate the presence of cracks and to clean the ampule.

V. PREPARATION OF SOLUTION.

A. *Amount to be prepared at one time.*—In marked contrast to the practice with arsphenamine, do not prepare any more solution at one time than can be administered within 20 minutes.

B. *Concentration.*—Preferably, 1 decigram should be dissolved in 12.5 c. c. of water. This solution is then twice as concentrated as an arsphenamine solution. Concentrations as high as 1 decigram in 0.5 c. c. of water can be used in the field, or under other special circumstances. The highly concentrated solutions, however, should be given very slowly.

C. *Solution:*

1. Put in Erlenmeyer flask 12.5 c. c. sterile distilled water for each decigram of neoarsphenamine. In the field the concentrated solution can be made in the ampule itself by using water supplied in another ampule. (*Caution:* The distilled water used must be at room temperature and not to exceed 30° C.)

2. Open ampule and sprinkle—do not dump—powder into the water and, by preference, allow it to go into solution with no agitation whatever. Slight rotation of the flask is permissible. *Shaking the solution increases its toxicity and should be avoided.*

IN CASE THE SOLUTION IS NOT PERFECTLY CLEAR AND TRANSPARENT, IT SHOULD UNDER NO CIRCUMSTANCES BE USED. WHETHER IT REQUIRES ONE MINUTE OR TEN MINUTES FOR THE DRUG TO FORM A PERFECT SOLUTION IS UNIMPORTANT, BUT IT

SHOULD NOT REQUIRE MORE THAN TEN MINUTES. THE IMPORTANT POINT IS, NOT THE *RATE* OF SOLUBILITY BUT THE *COMPLETE* SOLUBILITY OF THE DRUG.

3. As soon as the neoarsphenamine is in solution, *filter* through washed gauze into tall, narrow cylinders and keep stoppered. It is preferable to use a size of cylinder which the solution will nearly fill. The smaller the air column over the solution the less the danger of increased toxicity. The solution is now ready to inject, and, in marked contrast to the arsphenamine solution, which should stand at least 30 minutes before its injection, the neoarsphenamine solution should be injected *immediately*, and in no case shall it be allowed to stand longer than 20 minutes.

4. *Dosage.*—The initial dose, as a rule, should be small. The average dose is about 0.6 gram for 150 pounds body weight; but no attempts to lay down a hard and fast rule in this regard are made. The patient must be individualized.

VI. ADMINISTRATION.

The directions made under arsphenamine (p. 1875, VI) to apply the administration of neoarsphenamine, with the exception of the dosage, rate, and method of administration.

Rate.—If instructions haye been followed, the proper rate is practically insured by the character of the apparatus, but it must be checked by using a time-piece, and in no case, *whether the gravity or the syringe method is used, should more than 0.1 gram of neoarsphenamine be injected in 30 seconds*, or 0.6 gram in 3 minutes. This time is one-half that required for arsphenamine. In giving concentrated solutions, especial care is necessary in order to carry out this rule.

VII. REACTIONS.

See instructions under Arsphenamine, VII.

CONDENSED STANDARD INSTRUCTIONS FOR THE PREPARATION AND INTRAVENOUS ADMINISTRATION OF ARSPHENAMINE AND NEOARSPHENAMINE FOR THE MEDICAL DEPARTMENTS OF THE ARMY, OF THE NAVY, AND OF THE VETERANS' BUREAU, AND BY THE PUBLIC HEALTH SERVICE.

ARSPHENAMINE.

Reactions are usually due to errors in technique or failure to adapt treatment to needs of patient. Arsphenamine is preferable to neoarsphenamine.

I. Use any properly licensed product.

II. Use only the gravity method.

III. *Materials needed.*—Erlenmeyer flasks, glass funnels, graduated cylinders, sterile gauze, sterilized freshly distilled water, normal sodium hydroxide solution, graduated pipette or burette, and gravity apparatus, consisting of 300 c. c. gravity cylinder, pure gum rubber tubing about 40 inches length, diameter $\frac{5}{32}$ inch., end adapter, glass window, slip needles, 19 standard gauge, 1½-inch cannula, medium bevel, and pinch cocks.

IV. *Inspection of drug.*—Record name and lot number; note especially dosage, color, and mobility of powder. If ampules are cracked, or if powder is other than pale yellow to lemon color and not freely mobile, *do not use.*

V. *Preparation of solution.*—Prepare not more than enough for 10 patients at one time.

A. Immerse ampules in alcohol.

B. Place in Erlenmeyer flask about 10 c. c. distilled water at room temperature for each 0.1 gram of the drug to be used, open ampule and sprinkle powder—do not dump—on surface of water; allow to go into solution with little or no agitations.

Exception.—Arsenobenzol (D. R. I.) requires for rapid solution either the use of hot water alone or cold water after having been previously moistened with ethyl alcohol (1 c. c. to 0.6 gm.). In either case immediate, vigorous shaking for a few seconds is essential to prevent the formation of gummy masses. After shaking, wait for complete solution and cooling.

C. *Alkalinization.*—When solution is complete, add 0.85 normal alkali (U. S. P.) for each 0.1 gram of drug (e. g., 1 gm. requires 8.5 c. c.). When standardized normal sodium hydroxide is not avilable, see detailed instructions for procedure. *The drop method of measuring the alkali should never be used.*

D. *Filtration.*—Filter the clear, alkalinized, amber colored solution through sterile gauze, four-ply, previously washed out with distilled water, into a graduated cylinder (not the gravity cylinder).

E. *Dilution.*—Dilute with distilled water so that 0.1 gram arsphenamine is contained in 25 c. c. (e. g., 100 c. c. contains 0.4 gram.)

F. *Time of standing.*—The filtered, perfectly clear, alkalinized and properly diluted solution should now *stand for 30 minutes* before being injected.

G. *Dosage.*—The initial dose should be small. The average dose is about 0.4 gm., but in this respect each case should receive individual consideration. For radical cure, full doses are indicated.

VI. *Administration:*

A. *Preparation of patient.*—In each instance attention should be given to the physical condition, effects of previous treatments of arsphenamine, etc.

B. The use of gravity apparatus, with level of fluid 3 feet above the vein, and 19 gauge needle should give proper rate of injection. However, it should be checked by a timepiece and not more than 25 c. c. (0.1 gm. of drug) should be injected per minute. It is advisable to take about 5 minutes for injection of the average dose (0.4 gm.).

VII. *Reactions.*—See detailed instructions.

NEOARSPHENAMINE.

I. Use any properly licensed product.

II. The gravity method of injection is strongly recommended, in view of the fact that reactions have occurred much less frequently in large clinics using this method as compared with large clinics using the syringe method. The syringe method, however, is a valuable one especially in the field. If the syringe is used, it should be with a 25-gauge needle connected to the syringe with a short piece of rubber tubing.

III. *Materials needed.*—Gravity apparatus, as for arsphenamine, or 10 to 50 c. c. all-glass syringes, with 25-gage needles and short rubber connections. Erlenmeyer flasks, funnels, sterile gauze, cylinders, and sterile freshly distilled water.

IV. *Inspection of drug* is even more important than in case of arsphenamine, as neoarsphenamine may, under certain conditions, change in the ampule. Note manufacturer, amount contained, and especially color, mobility, and bulk of the powder. If ampules are cracked, or if powder is other than canary yellow and not freely mobile, *do not use.*

V. *Preparation of solution:*

A. Immerse ampules in alcohol.

B. Place in an Erlenmeyer flask, 12.5 c. c. of distilled water for each 0.1 gram of the drug to be used, and sprinkle—do not dump—powder on the surface of the water. Allow it to go into solution without shaking. Slight agitation by rotating the flask is permissible. *Shaking increases toxicity.* While in the field and under special circumstances a concentration as high as 0.1 gram in 0.5 c. c. of water can be used, the use of 12.5 c. c. to each 0.1 gram is strongly recommended. *Discard any product which is incompletely soluble.*

C. *Filtration.*—Filter the perfectly clear solution through washed sterile gauze into a narrow graduated cylinder.

D. *Time of standing.*—Neoarsphenamine solutions, in marked contrast to arsphenamine solutions, should not stand but should be given at once, and *in no case should they be allowed to stand for more than 20 minutes. If any haziness or clouding occurs, do not use.*

E. *Dosage.*—The initial dose should be small. The average dose is 0.6 gm., but in this respect each patient should receive individual consideration.

VI. *Administration.*—Pay particular attention to preparation of patient and to rate of injection, which must not exceed the introduction of more than 0.1 gm. of neoarsphenamine in 30 seconds, whether the gravity or the syringe method be employed. The rate may be almost perfectly controlled by the use of the gravity apparatus specified. With the syringe method the use of the small sized needle specified and the short rubber tube connector will enable one to inject sufficiently slowly without great difficulty, although greater care is necessary than with the gravity method. The rate should be frequently checked with a timepiece.

VII. *Reactions.*—See detailed instructions.

THE COLLEGE STUDENT AND VENEREAL DISEASES.

WHAT COLLEGE PRESIDENTS SAY.

Is venereal infection decreasing among college students? Rather definite answers to this query came as an interesting sidelight in response to a recent effort on the part of the United States Bureau of Education and the United States Public Health Service to obtain from college presidents their opinions with respect to the prevailing attitudes and practices of college men in sexual matters. Nearly one hundred college and university executives were asked the following questions:

> In your experience does it seem that the student's attitude toward sexual promiscuity, or his habits and practices have undergone any considerable change during the past 15 years? If so, what is the direction of the change and to what forces do you attribute it?[1]

In all, 65 replies were received, embracing comments on a variety of matters, such as the apparent growing familiarity between the sexes, the effect of the war and contact with European standards upon sex conduct, the prevailing fashions in dress, the modern dance forms, the conversational habits of students, and the prevalence of venereal diseases and the attitude of college men toward them. These various problems of conduct, directly or remotely related to sex, are discussed, as might be expected, from many points of view. What one college president sees as a sign of relaxed moral standards another views simply as a symptom of an effort to place sex relation-

---

[1] The questions, it will be noted, make no reference to venereal diseases.